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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/854,204	05/11/2001	Peter Martin Fischer	CCI-010DV	8487

959 7590 11/07/2003

LAHIVE & COCKFIELD  
28 STATE STREET  
BOSTON, MA 02109

EXAMINER
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CANELLA, KAREN A

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 11/07/2003

16

Please find below and/or attached an Office communication concerning this application or proceeding.

**Office Action Summary**

Application No.

09/854,204

Applicant(s)

FISCHER ET AL.

Examiner

Karen A Canella

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☐ Claim(s) 1 and 49-75 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☐ Claim(s) 1, 49-75 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on \_\_\_\_ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

**Priority under 35 U.S.C. §§ 119 and 120**

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

**Attachment(s)**

- 1) ☒ Notice of References Cited (PTO-892)                      4) ☐ Interview Summary (PTO-413) Paper No(s). \_\_\_\_.
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)                      5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) \_\_\_\_.
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION.**

1. Claims 1, 53, 54, 58, 60-71 have been amended. Claims 72-75 have been added. Claims 1 and 49-75 are under consideration. After review and reconsideration, the species election of paper no. 8 has been withdrawn.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.
3. Claims 1, 51 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Kalderon et al (Cell, 1984, Vol. 39; pp. 499-509) or Feigl et al (In: Struct. Act. Nat. Pept. Proc., 1981, pp. 523-538) or Janmey et al (WO 98/20887). Claim 1 is drawn in part to a membrane translocation peptide carrier moiety consisting of RRMKWKK (SEQ ID NO:2), wherein one or more amino acids are replaced by naturally occurring amino acids. Claim 51 embodies the carrier moiety of claim 1 wherein one or more amino acids are replaced by non-homologous replacement. Claim 60 embodies the carrier moiety of claim 1 wherein one or more residues at any of positions 1-5, 6 or 7 of SEQ ID NO:2 are replaced by naturally occurring or non-naturally occurring amino acids.

Kalderon et al disclose a peptide transport sequence consisting of PKKKRKV which transports proteins into the nucleus (page 505, second column, lines 19-24). Because transport into the nucleus requires traversing the nuclear membrane, the PKKKRKV sequence is a membrane translocation sequence. An examination of PKKKRKV relative to SEQ ID NO:2 indicates that PKKKRKV represents non-homologous replacement of amino acids relative to SEQ ID NO:2

Feigl et al disclose Viridogriseln I (page 523, Figure 1) wherein said Viridogriseln consists of natural and non-natural amino acid substitutions of SEQ ID NO:2. Feigl et al disclose that transport cations across membranes (page 525, second full paragraph, lines 7-11). Thus Viridogriseln is a membrane translocation carrier moiety as it transports cations across membranes.

Janmey et al disclose the peptide of SGLKYKK (SEQ ID NO:6) and FQVKGR (SEQ ID NO:11) which binds PPI and therefore useful for the transport of an extracellular agent

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across a cell membrane (page 7, lines 4-10, and lines 26-31, and page 8, lines 8-10, Tables 1 and 2 and page 16, lines 8-11), thus fulfilling the specific embodiments of membrane translocation peptide. Both SEQ ID NO:6 and 11 are 7-mer peptides, thus fulfilling the specific embodiments of consisting of SEQ ID NO:2 wherein one or more amino acids are replaced by naturally occurring amino acids.

4. Claims 1, 51, 53 and 60 are rejected under 35 U.S.C. 102(b) as being anticipated by Borchardt et al (In: Medicinal chemistry: Today and Tomorrow, Proceedings Symposium, 1997, pp. 191-196). The specific embodiments of claims 1, 51, 60, 62 and 63 are set forth above. It is noted that claim 1 is also drawn in part to a membrane translocation peptide carrier moiety comprising SEQ ID NO:2, wherein one or more amino acids are replaced by a naturally or non-naturally occurring amino acid residue, in combination with a spacer group present between any two amino acid residues (sections b, e and h). Claim 53 embodies the carrier moiety of claim 1 wherein the replacement amino acid is the non-natural amino acid of lactic acid.

Borchardt et al disclose that transcellular permeation of a solute requires interaction of said solute with the membrane, and that the ability of a peptide to transverse the membrane barrier requires interaction with the lipid bilayer and integral and peripheral membrane proteins (page 193, lines 1-8). Borchardt et al disclose the cyclic peptide (last entry in Table 1 on page 194) which consist of the hexapeptide WAGGDA wherein the W is substituted with lactic acid, fulfilling the specific embodiment of claim 1 drawn to substitution with natural and unnatural amino acids and the specific embodiment of claim 53 which specifies lactic acid as an unnatural amino acid. Further, the cyclic peptide disclosed by Borchardt et al comprises an aryl group as a linker molecule between the lactic acid and the C-terminal Ala residue. Borchardt et al disclose that said cyclic peptide had an increased ability to permeate layers of Caco cells (page 194, lines 10-14) thus fulfilling the specific embodiment of a membrane translocation.

5. The provisional rejection of claims 1, 47 and 49-66 under the judicially created doctrine of obviousness-type double patenting is maintained for reasons of record. New claims 72-75 are also rejected for the same reasons of record. Acknowledgement is made of applicants intent of filing a terminal disclaimer when allowable subject matter is indicated.

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6. Claims 1 and 49-75 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-29 of U.S. Patent No. 6,472,507. Although the conflicting claims are not identical, they are not patentably distinct from each other because it would be obvious to attach the instant membrane translocation peptide carrier moieties to drug moieties in order to direct drugs into the internal milieu of cells.

7. All other rejections and objections as set forth in Paper No.16 are withdrawn.

### *Conclusion*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Karen Canella whose telephone number is (703) 308-8362. The examiner can normally be reached on Monday through Friday from 8:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3995. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

  
Karen A. Canella, Ph.D.

Patent Examiner, Group 1642

11/03/03